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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/996,838	11/29/2001	Hans Hofland	P 23,643-A USA	6395

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EXAMINER	
EPPS FORD, JANET L	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 09/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/996,838	HOFLAND ET AL.	
	Examiner	Art Unit	
	Janet L. Epps-Ford	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7,11,14,15 and 18-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7,11,14,15 and 18-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 March 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7-13-2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7-13-05 has been entered.

2. Applicants have cancelled claims 2 to 6, 8 to 10, 12-13, and 16-17. Applicants have added new claims 20-32. Claims 1, 7, 11, 14-15, 18-32 are currently pending.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. The rejection of claim 1 under 35 USC 102(e) is withdrawn in response to Applicant's amendment of this claim.

Claim Rejections - 35 USC § 102/§ 103

5. Claims 1, 7, 11, 14-15, 18-19, remain rejected and new claims 20-23, and 30 are rejected under 35 U.S.C. 102(e) as being anticipated by Monahan et al., or unpatentable over Monahan et al. for the reasons of record set forth in the Final Office Action mailed 3-09-05.

Applicant's arguments filed 7-11-2005 have been fully considered, but they are not persuasive. In the response filed 7-11-2005, Applicants argued that the claims as amended distinguish over Monahan et al. in that they recite a colloid (or method for

making or using the same) which comprises a DNA-containing complex in which citraconic anhydride (CCA) or N-hydroxy succinimide (NHS) acetate has been reacted with the cationic lipids or polymers of the complex.

According to Applicants Monahan et al. does not disclose the reaction of anything with the cationic lipids of the DNA-containing complex described therein, but rather teaches the electrostatic interaction of anionic polymers with the cationic lipids in a recharging process. Furthermore, Applicants argue that Monahan et al. teach only the use of CCA and NHS ester in forming the above referenced anionic polymers and not for reacting with cationic lipids, and the NHS ester is used as a cross-linking agent, and CCA is used to react with cationic polymers to form anionic polymers.

Applicant's arguments are not persuasive because Monahan et al. clearly teach that the addition of citraconic anhydride to the cationic polymer poly-L-lysine, and the formation of citraconylpoly-L-lysine, and the addition of this compound to a complex of DNA and poly-L-lysine, wherein the overall zeta potential of the formed particles of this reaction is negative (see col. 25, lines 27-65). Moreover, as stated by Applicants above, Monahan et al. teach the use of NHS ester to react with cationic polymers to form anionic polymers. Additionally, it is clear that the invention of Monahan et al. is specifically designed for modifying DNA-polymer complexes to comprise a negative zeta potential for the express purpose of delivering nucleic acid in cells (see abstract). Therefore, contrary to Applicant's assertions, the invention set forth in Monahan et al. is considered to anticipate claims 1, 7, 11, 14-15, 18-19, and new claims 20-23.

Additionally, new claim 30, which recites that the complex further comprises a folate ligand as a targeting ligand is taught by Monahan et al. at col. 6, line 8.

6. Claims 1, 7, 11, 14-15, 18-19, remain rejected and new claims 20-23, and 28-30 are rejected under 35 USC § 103(a) as being unpatentable over Semple (US Patent No. 6,287,591 B1) taken with Trubetskoy (US 2003/0026841 A1) and Monahan et al. (6,379,966), for the reasons of record set forth in the Final Office Action mailed 3-09-2005.

Applicant's arguments filed 7-13-05 have been fully considered but they are not persuasive. Applicants traverse the instant rejection on the grounds that there is no motivation to combine the recites references to make the claimed invention. Specifically, Applicants argue that Examiner's rationale for making the instant rejection is based upon the incorrect belief that Monahan et al. discloses using NHS ester and CCA as reagents to modify the surface potential of DNA-containing complexes. According to Applicants Monahan et al. does not contain such a disclosure and neither do the other recited references. Therefore, according to Applicants the skilled artisan would not have been motivated to use NHS ester or CCA to modify the surface potential of the DNA-containing complexes of Semple et al.

Applicant's arguments are not persuasive because, the invention of Monahan et al. is drawn to methods for modifying DNA-polymer complexes to comprise a negative zeta potential for the express purpose of delivering nucleic acid in cells (see abstract). In specific a embodiment, Monahan et al. teach that the addition of citraconic anhydride to the cationic polymer poly-L-lysine, and the formation of citraconylpoly-L-lysine, and

the addition of this compound to a complex of DNA and poly-L-lysine, wherein the overall zeta potential of the formed particles of this reaction is negative (see col. 25, lines 27-65). Moreover, as stated by Applicants above, Monahan et al. teach the use of NHS ester to react with cationic polymers to form anionic polymers.

Again, contrary to Applicant's assertions, one of ordinary skill n the art would have been motivated to modify the DNA-lipid compounds of Semple et a. with the teachings of Monahan et al. because this reference teaches the treatment of cationic polymers with CCA and NHS ester to confer a negative charge in the design of DNA-lipid complex for delivery into a cell. Furthermore, Trubetskoy teaches that an addition of polyanionic molecules to a lipid/DNA complex would enhance the transfer activity of a DNA/cationic lipid complex.

Furthermore, new claim 30, which recites that the complex further comprises a folate ligand as a targeting ligand is taught by Monahan et al. at col. 6, line 8. Additionally, new claims 28-29 which recites wherein the cationic lipid contains hydrophobic moieties which are based one or more acyl chains of various lengths, or wherein said cationic lipid contains a hydrophobic moiety which is a myristyl chain or palmityl chain. These limitations are clearly rendered obvious over the cationic lipids described in Semple et al. at col. 11, wherein it states that amino lipids containing unsaturated fatty acids with carbon chain lengths in the range of C14 to C22 (which encompasses both myristyl and palmityl hydrophobic groups) are particularly preferred in the design of the DNA lipid complexes described by Semple et al.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 24-27 and 31-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. 24-27 and 31-32 recites the limitation "the process" in claim 19. There is insufficient antecedent basis for this limitation in the claim. Claim 19 recites a method for gene therapy, the claim does not recite a process as recited in claim 1 for making a stable colloid. Perhaps Applicants intended for these claims to depend from claim 1.

10. It is noted that the instant rejection could have been made final, however due to the presence of limitations recited in claims 28-30, that were not previously considered by the examiner, the instant rejection is made non-final.

11. No claims are allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 9:30 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave T. Nguyen can be reached on 517-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Janet L. Epps-Ford
Examiner
Art Unit 1633

JLE